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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> C12N 15/18, 15/79, 5/06, C07K 14/475, 16/18, C12P 21/02, A61K 38/18, G01N 33/53		<b>A3</b>	<b>(11) International Publication Number:</b> WO 98/24811 <b>(43) International Publication Date:</b> 11 June 1998 (11.06.98)
<b>(21) International Application Number:</b> PCT/US97/20888 <b>(22) International Filing Date:</b> 20 November 1997 (20.11.97) <b>(30) Priority Data:</b> 08/759,657 6 December 1996 (06.12.96) US 08/933,455 18 September 1997 (18.09.97) US <b>(71) Applicant:</b> ZYMOGENETICS, INC. [US/US]; 1201 Eastlake Avenue East, Seattle, WA 98102 (US). <b>(72) Inventors:</b> GILBERT, Teresa; 246 12th Street S.E., Seattle, WA 98002 (US). CONKLIN, Darrell, C.; Apartment 2, 2332 Minor Avenue East, Seattle, WA 98102 (US). HART, Charles, E.; 20114 183rd Place N.E., Woodinville, WA 98072 (US). NYGAARD, Sean; 13625 S.E. 44th Street, Bellevue, WA 98006 (US). SHEPPARD, Paul, O.; 20717 N.E. 2nd Street, Redmond, WA 98053 (US). <b>(74) Agent:</b> PARKER, Gary, E.; ZymoGenetics, Inc., 1201 Eastlake Avenue East, Seattle, WA 98102 (US).			<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>  <b>(88) Date of publication of the international search report:</b> 1 October 1998 (01.10.98)
<b>(54) Title:</b> VASCULAR ENDOTHELIAL GROWTH FACTOR  <b>(57) Abstract</b>  Growth factors, their component polypeptides, methods of making them, polynucleotides encoding them, and methods of using them are disclosed. The growth factors are homodimeric or heterodimeric proteins having component polypeptide chains that each comprises a sequence of amino acid residues that is at least 80 % identical in amino acid sequence to residues 109 to 197 of SEQ ID NO:2. The growth factors are mitogenic for fibroblasts and smooth muscle cells, and may be used therapeutically or <i>in vitro</i> to stimulate cell growth, or to develop inhibitors of cell growth.			

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/20888

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/18 C12N15/79 C12N5/06 C07K14/475 C07K16/18  
C12P21/02 A61K38/18 G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	YAMADA, Y. ET AL.: "Molecular cloning of a novel Vascular Endothelial Growth Factor, VEGF-D" GENOMICS, vol. 42, no. 3, 15 June 1997, pages 483-488, XP002073018 see page 484 - page 485; figure 1 *'Materials and Methods' and 'Results'* --- -/--	1-4,8, 14-17, 21-26

☒ Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search

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International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>WO 97 12972 A (UNIVERSITA 'DEGLI STUDI DI SIENA) 10 April 1997</p> <p>see page 3, line 13 - line 18  see page 7, line 4 - page 9, line 26  see page 10, line 7 - line 22  see page 11, line 31 - line 37  see page 17, line 29 - page 19, line 16  see page 22, line 3 - page 27, line 11;  figures 1,2</p> <p style="text-align: center;">---</p>	<p>1-3,5,6,  9-11,  14-27,  29-32</p>
X	<p>ORLANDINI, M. ET AL.: "Identification of a c-fos-induced gene that is related to the platelet-derived growth factor/vascular endothelial growth factor family"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,  vol. 93, October 1996, WASHINGTON US,  pages 11675-11680, XP002029340</p>	<p>1-3,5,6,  9-11,14,  15,18,  21-27,  29-32</p>
Y	<p>see the whole document</p>	<p>7,28</p>
Y	<p>NILSSON, B. ET AL.: "Expression and purification of recombinant insulin-like growth factors from Escherichia coli"</p> <p>METHODS IN ENZYMOLOGY,  vol. 198, 1991,  pages 3-16, XP002073019  cited in the application  see page 5 - page 7  *Fusions to Staphylococcal Protein A*  see figures 1-3</p> <p style="text-align: center;">---</p>	<p>7</p>
Y	<p>WO 96 26736 A (LUDWIG INSTITUTE FOR CANCER RESEARCH) 6 September 1996</p>	<p>28</p>
A	<p>see page 8, line 1 - line 5</p> <p>see page 15, line 33 - line 36; example 16</p> <p style="text-align: center;">-----</p>	<p>1-27,  29-32</p>

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/20888

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9712972 A	10-04-1997	AU 7142996 A EP 0853668 A	28-04-1997 22-07-1998
WO 9626736 A	06-09-1996	US 5607918 A AU 5302196 A CA 2211687 A EP 0814827 A NO 973933 A	04-03-1997 18-09-1996 06-09-1996 07-01-1998 01-09-1997